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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/705,262	11/12/2003	Steve Warrington	WARRINGTON1	3198

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/705,262	WARRINGTON ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-6 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-6 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 12 November 2003 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 05172004.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Double Patenting

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 1-2 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-5 and 12-13 of copending Application No. 09/832,818. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-2 are drawn to a method for treating an individual with IB-MECA to achieve a therapeutic effect, the method comprises administering to the individual a dose of IB-MECA in an amount and for a time such as to achieve a maximal blood of less than about 160 nM. Claim 2 is limited to oral administration.

The method of claims 1-2 differ from the invention of the '818 application in that the '818 application is not limited to the use of IB-MECA; however, since the '818 application is drawn to the use of a very limited number of compounds one of ordinary skill in the art at the time of the invention would have readily envisioned using IB-MECA in the method of the '818 application. Although the '818 application does not explicitly claim orally administering IB-MECA, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to employ oral administration since the '818 application teaches that it is a preferred mode of administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

3. Claims 1-6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-14 and 28 of copending Application No. 10/715,823. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-6 are drawn to a method for treating an individual with IB-MECA to achieve a therapeutic effect, the method comprises administering to the individual a dose of IB-MECA in an amount and for a time such as to achieve a maximal blood of less than about 160 nM. Claim 2 is limited to oral administration. Claims 3-6 limit the dosage.

The method of claims 1-6 differ from the invention of the '823 application in that the '823 application is not limited to the use of IB-MECA; however, since the '823 application is drawn to the use of a very limited number of compounds one of ordinary

skill in the art at the time of the invention would have readily envisioned using IB-MECA in the method of the '823 application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 1-6 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 49, 56 and 64 of copending Application No. 09/700,751. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 1-6 are drawn to a method for treating an individual with IB-MECA to achieve a therapeutic effect, the method comprises administering to the individual a dose of IB-MECA in an amount and for a time such as to achieve a maximal blood of less than about 160 nM. Claim 2 is limited to oral administration. Claims 3-6 limit the dosage.

The method of claims 1-6 differ from the invention of the '751 application in that the '751 application is not limited to the use of IB-MECA; however, since the '751 application is drawn to the use of a very limited number of compounds one of ordinary skill in the art at the time of the invention would have readily envisioned using IB-MECA in the method of the '751 application. Although the '751 application does not explicitly claim orally administering IB-MECA, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to employ oral administration since the '751 application teaches that it is a preferred mode of administration.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-6 are drawn to a method for treating an individual; however, the claims fail to set forth what condition(s) are to treated. In the absence of the conditions treated or patient population, one of ordinary skill in the art at the time of the invention would not be apprised of the metes and bounds of the invention.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobsen et al. US 5,773,423 (Jacobsen).

Jacobsen discloses compounds which have been found to be selective A_3 adenosine receptor agonists, pharmaceutical compositions containing such compounds, and related treatment methods and assay methods (column 2, line 59 to column 3, line 33). The modification of adenosine at the 5'-position and/or at the N^6-position with groups that enhance A_3 potency has been found to result in moderate A_3 selectivity. In particular, the 5'-methyluronamide modification of adenosine and the N^6-benzyl group, either alone or in combination, increases affinity in binding to A_3 receptors relative to A_1 and A_{2a} receptors. Optimization of substituent groups has led to the development of the highly potent A_3 agonist N^6-(3-iodobenzyl)-adenosine-5'-N-methyluroamide (IB-MECA) which is 50-fold selective for A_3 vs. either A_1 or A_2 receptors. Disease states and conditions that may be chronically treated include inflammatory disorders, Parkinson's disease, cardiac disease, and contraception (column 25, line 20 to column 26, line 19). One skilled in the art will recognize that dosage will depend upon a variety of factors including the strength of the particular compound employed, the age, species, condition, and body weight of the animal, as well as the severity/stage of the disease or condition (column 26, line 61 to column 27, line 23). The size of the dose will also be determined by the route, timing, and frequency of administration as well as the existence, nature, and extent of any adverse side effects that might accompany the administration of a particular compound and desired physiological effect. Exemplary dosages range from about 0.1 to about 100 mg/kg body weight of the animal being treated/day. Therapeutically effective dosages range from about 0.01 to about 10 mg/kg body weight/day. There are a wide variety of suitable formulations including formulations for

oral, aerosol, parenteral, subcutaneous, intravenous, intramuscular, interperitoneal, rectal, and vaginal administration (column 19, lines 59-67).

9. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by Jacobsen et al. US 5,688,774 (Jacobsen).

Jacobsen discloses compounds which have been found to be selective A_3 adenosine receptor agonists, pharmaceutical compositions containing such compounds, and related treatment methods and assay methods (column 3, line 3 to column 4, line 48). The modification of adenosine at the 5'-position and/or at the N^6-position with groups that enhance A_3 potency has been found to result in moderate A_3 selectivity. In particular, the 5'-methyluronamide modification of adenosine and the N^6-benzyl group, either alone or in combination, increases affinity in binding to A_3 receptors relative to A_1 and A_{2a} receptors. Optimization of substituent groups has led to the development of the highly potent A_3 agonist N^6-(3-iodobenzyl)-adenosine-5'-N-methyluroamide (IB-MECA) which is 50-fold selective for A_3 vs. either A_1 or A_2 receptors. Disease states and conditions that may be chronically treated include inflammatory disorders, Parkinson's disease, cardiac disease, and contraception (column 12, line 13 to column 14, line 4). One skilled in the art will recognize that dosage will depend upon a variety of factors including the strength of the particular compound employed, the age, species, condition, and body weight of the animal, as well as the severity/stage of the disease or condition. The size of the dose will also be determined by the route, timing, and frequency of administration as well as the existence, nature, and extent of any adverse side effects that might accompany the administration of a particular compound and desired

physiological effect. Exemplary dosages range from about 0.1 to about 100 mg/kg body weight of the animal being treated/day. Therapeutically effective dosages range from about 0.01 to about 10 mg/kg body weight/day. There are a wide variety of suitable formulations including formulations for oral, aerosol, parenteral, subcutaneous, intravenous, intramuscular, interperitoneal, rectal, and vaginal administration (column 10, lines 20-65).

10. Claims 1-4 and 6 are rejected under 35 U.S.C. 102(b) as anticipated by Baharav et al. International Journal of Molecular Medicine, (2002) Vol. 10, No. Supplement 1, pp. S104, Meeting info: 7th World Congress on Advances in Oncology and the 5th International Symposium on Molecular Medicine, Hersonissos, Crete, Greece, October 10-12, 2002 (Baharev).

Baharev teaches the effect of adenosine and the A3 adenosine receptor agonist IB-MECA on joint inflammation and autoimmune disease models. A3 adenosine receptor (A3AR) activation inhibits the production of anti-inflammatory cytokines such as tumor necrosis factor-alpha (TNF), interleukin 12 and interferon-gamma. The aim of the study was to explore the effect of adenosine and its A3AR agonist, IB-MECA on the development of inflammatory reaction in different models of arthritis. Three experimental animal models were used: **a**) zymosan induced arthritis (ZIA) – adenosine (0, 0.25 and 0.5 mg/kg) was introduced intraperitoneally every second day; **b**) adjuvant arthritis (AA) – IB-MECA (10 or 100 μg/kg) was introduced orally every day, started seven days after immunization; **c**) a newly developed model for Behqet disease induced by tropomyosin, manifested by arthritis (TIA) – treatment as in **b**. Arthritis intensity was

evaluated clinically by knee swelling measurements and by histology. In the AA and TIA models a dose dependent anti-inflammatory effect was noted. Some of the treated animals did not develop clinical arthritis at all and the remainder animals had significantly milder synovitis.

Conclusion

11. Claims 1-6 are pending. Claims 1-6 are rejected. No claims are allowed.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on Monday - Friday 10 am to 3 pm (Maxi Flex).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Dr. Patrick T. Lewis
Primary Examiner
Art Unit 1623

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